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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/765,236	01/26/2004	Matthias Rath	11957/62	5789

7590 10/12/2006

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EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 10/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/765,236	RATH, MATTHIAS	
	Examiner	Art Unit	
	Brian S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-27 and 32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-27 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01/26/04* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. By Amendment filed July 13, 2006, claims 14-20 and 28-31 have been cancelled and claims 21 and 32 have been amended. Claims 21-27 and 32 are currently pending for prosecution on the merits of the case.

Summary of Action

2. The rejection of claims 14-20 under 35 U.S.C. 103(a) as being unpatentable over Rath et al. (US 5650418) in view of Rath et al. (EP 0 891771 A1) is not maintained in light of the applicant's cancellation of claims 14-20.

3. The rejection of claims 21-27 and 32 under 35 U.S.C. 103(a) as being unpatentable over Rath et al. (US 5650418) in view of Rath et al. (EP 0 891771 A1), and further in view of Chochran (US 6048846 A), Product Information Brochure (Life Extension Mix Multivitamin, 1997) and Umbdenstock (US 5332579) is maintained for the reasons of record.

4. Applicant's amendment requiring "2-Lasotene, Latein, Zea-Cryptoxanthin" in independent claim 21 necessitates a new ground of rejection in this Office Action.

Looking at the prosecution history of the parent application (09/970,609 filed 10/03/2001 which is patented USP 6,693,129) of the instant divisional application, Paper No. 8 (The Notice of Allowability) was issued on September 15, 2003 indicating the allowability of claims 9-13 and 28. Particularly claim 9, line 3, was amended with the language of ": α-carotene, lutein, zea-cryptoxanthin" to further define the term "carotenoid-mix" in the claim 9 by Examiner's Amendment (see page 2 of the Notice of Allowability mailed September 15, 2003).

However, due to a typographical error in 'printing' procedure, the claim 1 of USP 6,693,129, line 4, was printed with "2-Lasotene, Latein".

Applicant is advised to file the Certificate of Correction under 37 CFR 1.322 to correct the typographical error of "2-Lasoten, Latein" in the claim 1 of USP 6,693,129.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 21-27 and 32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claimed invention, particularly independent claim 21, introduces new limitation into the claimed invention, namely "2-Lasotene, Latein, Zea-Cryptoxanthin".

Although "zea-cryptoxanthin" is supported in the page 11, Table 1, lines 10-11, the examiner determines that when all evidences in the original disclosure are considered and carefully review, the term "2-Lasotene and Latein" fails to find support in the original specification.

As discussed in preceding comments, "2-Lasotene and Latein" recited in the present claims, which did not appear in the specification filed, introduces new concepts and violate the description requirement of the first paragraph of 35 USC 112.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 21-27 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claimed invention, particularly independent claim 21, recites "2-Lasotene, Latein". The term "2-Lasotene, Latein" is not recognized in the art and leaves the reader in doubt as to the meaning of the invention to which they refer, thereby rendering the definition of the subject-matter of said claims unclear.

As discussed above, in light of the parent application (USP 6,693,129), the term "2-Lasotene, Latein" is resulted from the 'printing' error. For the examination purpose, the term "2-Lasoten and Latein" is interpreted as "α-carotene, lutein, zea-cryptoxanthin".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

> such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. Claims 21-27 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rath et al. (US 5650418) in view of Rath et al. (EP 0 891771 A1), and further in view of Chochran (US 6048846 A), Product Information Brochure (Life Extension Mix Multivitamin, 1997) and Umbdenstock (US 5332579).

Rath (US'418) teaches use of 5-500mg/kg of lysine (i.e., lysine hydrochloride, lysine dihydrochloride, lysine orotate, lysine succinate or lysine glutamate) in combination with 5-2500 mg/kg of ascorbic acid (i.e., ascorbate, ascorbate salts) and 1-300mg/kg of niacin (nicotinic acid) for treating cardiovascular disease by lowering the plasma concentration of lipoprotein such as Lp(a) (column 2, lines 15-21 and 47-57; column 3, line 11 thru 32; Table I). The Rath also teaches that other vitamins and compounds with demonstrated antioxidative properties (e.g., tocopherol and beta-carotene) could be added to the said combination (column 3, lines 54-59 and column 4, lines 19-23).

Rath (EP'771) teaches use of 5-1000mg/kg of lysine (i.e., lysine hydrochloride, lysine dihydrochloride, lysine orotate, lysine succinate or lysine glutamate) in combination with 5-5000mg/kg of ascorbic acid (i.e., ascorbate), 5-1000 mg/kg of proline (i.e., proline

hydrochloride, proline dihydrochloride, proline orotate, proline succinate and proline glutamate) and vitamin D for treating cardiovascular disease by lowering the plasma concentration of lipoprotein such as Lp(a) (page 4, lines 12-45; column 5, lines 3-7; Table I). The Rath also teaches that N-acetylglucosamine and other essential nutrients, that is minerals, trace elements or amino acids, can be added to the said combination (abstract; page 4, lines 47-48).

Cochran teaches a combination of biochemical substances comprising l-arginine, l-lysine, l-proline, l-cysteine, l-carnitine, ascorbic acid (vitamin C), vitamin E (e.g., d-alpha-tocopherol, alpha-, beta- and gamma-tocopherol), beta-carotene, carotenoid mix, thiamine, riboflavin, pyridoxine, cobalamin, niacinamide, niacin, inositol, colecalciferol (vitamin D), biotin, folic acid, citrus biofavonoids, co-enzyme Q-10, calcium, potassium, magnesium, manganese, zinc and chromium, wherein said biochemical composition is effective in lowering total cholesterol, LDL cholesterol and trigycerides (column 4, lines 62 thru column 5, line 8; column 10, lines 15-47; column 19, lines 21-30; Figures 1 and 5-8; Claims).

Commercially available Life Extension Mix Multivitamin discloses a multi-vitamin comprising ascorbic acid, ascorbyl palmitate, D-alpha tocopherol, ascorbic acid, thiamin, cholecalciferol, riboflavin, niacin, niacinamide, magnesium ascorbate, pyridoxine, folic acid, cyanocobalamin, D-calcium panthothenate, calcium ascorbate, dicalcium phosphate, calcium glucarate, biotin, magnesium glycinate, magnesium ascorbate, zinc, l-selenomethionine, copper, manganese, chromium, molybedenum, lysine, cysteine, inositol, citrus bioflavonoid and grape seed extract (pynogenol or Leucoselect).

Umbdenstock teaches or suggests a nutritional supplement comprising Vitamin A, beta-carotene, vitamin B1, vitamin B6, vitamin B12, niacin, niacinamide, vitamin C, biotin,

pantothenic acid, inosito, amino acid, magnesium glycinate, manganese glycinate, chromium glycinate, zinc glycinate, copper glycinate, potassium glycinate and molybdenum glycinate (column 7, lines 55-57; column 8, lines 32-64; column 9, line 47 thru column 10, line 23; Claims).

The teaching of Rath'418 differs from the claimed invention in use of ascorbic acid, niacin, lysine, proline and secondary ingredients (e.g., beta-, gamma-, delta-, tocopherol-mix, beta-carotene, biotin, calcium ascorbate, calcium glycinate, carotenoid mix, cholecalciferol, chromium glycinate, citrus bioflavonoids, coenzyme Q10, copper glycinate, cyanocobalamin, d-alpha-tocopherol, di-calcium pantothenate, dicalcium phosphate, folic acid, inositol, l-arginine, l-carnitine, l-cysteine, l-selenomethionine, magnesium ascorbate, magnesium glycinate, manganese chelate, molybdenum glycinate, potassium chelate, pycnogenol, pyridoxine, riboflavin, thiamine and zinc glyconate) in a composition, (ii) the lowering of total cholesterol, LDL-cholesterol, triglycerides, low density lipoprotein and homocystein, and (iii) the specific plasma concentration level of the lipoprotein lowered by the administration of said combination. To incorporate such teaching into the teaching of Rath'418, would have been obvious in view of Rath (EP'771) who teaches the use of proline in composition in treating cardiovascular disease by lowering the plasma concentration of lipoprotein such as Lp(a), the commercially available "Life Extension Mix Multivitamin" that teaches the use of ascorbyl palmitate, magnesium ascorbate, dicalcium phosphate, magnesium glycinate, grape seed extracts (pynogenol) in a nutritional multi-vitamin supplement, and Umbdenstock who teaches the use of manganese glycinate, chromium glycinate, zinc glycinate, copper glycinate, potassium chelate (potassium glycinate) and molybdenum glycinate in a nutritional supplement.

Above references in combination make clear that ascorbic acid, niacin, lysine and proline have been individually used for cardiovascular disease by modifying the plasma concentration of the lipoprotein in a mammal. It is obvious to combine two compositions each of which is taught by prior art to be useful for same purpose; idea of combining them flows logically from their having been individually taught in the prior art. The combination of active ingredient with the same character is merely the additive effect of each individual component. *See In re Kerkhoven, 205 USPQ 1069 (CCPA 1980).*

In addition, above references in combination make clear that vitamin C (e.g., ascorbic acid, ascorbyl palmitate), Vitamin E(e.g,, beta-, gamma-, delta-tocopherol-mix, d-alpha-tocopherol), vitamin A (e.g., beta-carotene, carotenoid mix), vitamin D (e.g., cholecalciferol), vitamin B1 (e.g., thiamine), vitamin B2 (e.g., riboflavin), vitamin B3 (e.g., niacin, niacinamide), vitamin B5 (e.g., d-calcium panthothenate), vitamin B6 (e.g., pyridoxine), vitamin B12 (e.g., cyanocobalamin), folic acid, biotin, inositol, L-arginine, L-carnitine, L-cysteine, L-proline, L-selenomethionine, calcium ascorbate, calcium glycinate, chromium glycinate, citrus bioflavonoids, coenzyme Q10, copper glycinate, cyanocobalamin, dicalcium phosphate, magnesium ascorbate, magnesium glycinate, manganese chelate, molybdenum glycinate, pycnogenol, potassium chelate and zinc glycinate are well known ingredients that are readily recognized in a nutritional supplement art.. Above references in combination makes clear that the formulation of the claimed composition is well within the skill of the artisan. One would have been motivated to make such modification to increase the efficacy by making the formulation in additive or synergistic combination of known nutrients. Although the instant claims use the

different names for the said ingredients than those taught in the cited references, these references are particularly pertinent and relevant because all the claimed species and their roles are well taught in the cited reference. Thus, one would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities, and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

With respect to the specific dosage amounts of ascorbic acid, niacin, lysine and praline in said composition, determination of the appropriate dosage for treatment involving each of the above mentioned formulations is routinely made by those of ordinary skill in the art and is within the ability of tasks routinely performed by them without undue experimentation, especially in light of the dosage information disclosed in the prior art. Hence, the reference makes obvious the instant invention. With respect to the lowering of "total cholesterol, LDL-cholesterol, triglycerides, low density lipoprotein and homocystein", such feature is considered to be expected feature of the prior art in references since the administration of said combination to the mammal in overlapping dosage amounts as to the instant invention would automatically achieve the desired effect of the instant invention, absence evidence to the contrary.

With respect to the specific plasma concentration of the lipoprotein, those of ordinary skill in the art would have been readily determine the desired plasma concentration of the lipoprotein for the therapeutic treatment of cardiovascular patient as determined by good medical practice.

With respect to the specific dosage amounts of ascorbic acid, niacin, lysine and praline in said composition, determination of the appropriate dosage for treatment involving each of the

above mentioned formulations is routinely made by those of ordinary skill in the art and is within the ability of tasks routinely performed by them without undue experimentation, especially in light of the dosage information disclosed in the prior art. Hence, the reference makes obvious the instant invention.

Although the instant claims use the different names for the said ingredients than those taught in the cited references, these references are particularly pertinent and relevant because all the claimed species and their roles are well known in the prior art. Thus, one would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

Response to Arguments

8. Applicant's arguments filed July 13, 2006 have been fully considered but they are not persuasive.

Applicant's argument in the response takes the position that the composition of the '418 patent or EP'771 would increases the plasma concentration of lipoprotein(a) by stimulating its release from arterial walls. Thus, the 418' patent would not teach or suggest the claimed methods to skilled artisan.

This argument is not found persuasive. As clearly indicated by USP'418 and EP'771 (see column 1, lines 63-65 of USP'418 and page 2, lines 19-21 of EP'771), it was widely known at the time of the invention was made that high levels of Lp(a) are associated with a high incidence of cardiovascular diseases. Furthermore, at the time of the invention was made, L-proline and

lysine analogs were known to interfere or inhibit with LDL binding to Lp(a) and apo(a), and reduce plasma levels of Lp(a) (see "A quantitative assay for the non-covalent association between apoliporotein[a) and apolipoprotein B: an alternative measure of Lp[a] assembly", Journal of Lipid Research, Vol. 41, 2000, pp. 1013-1019 in the considered PTO 1449). Thus, based on the USP'418 and EP'771, one having ordinary skilled in the art would have known that the referenced composition(s) is/are effective in treating cardiovascular disease (which is known to be associated by high level of Lp(a)) by inhibiting binding of Lp(a) and ultimately plaque formation, not by increasing the levels of Lp(a) alleged by the applicant. Reading the whole context of the cited references, one having ordinary skill in the art would have understood that the therapeutic effect (treatment of cardiovascular effects) of the composition is mediated by inhibiting binding potential of Lp(a), ultimately lowering the plasma level of lipoproteins.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

Conclusion

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. No Claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system,

see http://pair-direct.uspto.gov Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

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